ACCESS DB # 152875

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Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: MARK BERCH Examiner # : 59193 Date: 5/18/05

Art Unit: 1624 Phone Number: 2- 0663 Serial Number: 10625317

Location (Bldg/Room#): 5C01 (Mailbox #): 5C18 Results Format Preferred (circle): PAPER DISK

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following: MPEP

Title of Invention: _____

Inventors (please provide full names): _____

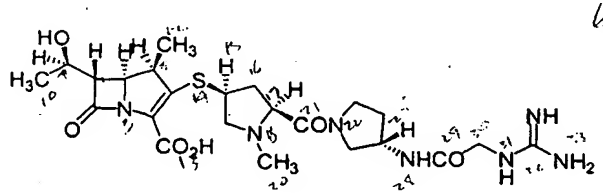
_____

Earliest Priority Date: _____

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*



This exact cmpd – no forseeable, but can be multicomponent version

Must the multicomponent

No hits at all, re-run without multicomponent

Need all Bibs with Synthesis of this compound

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STAFF USE ONLY

Searcher: Beverly 2528

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: _____

Date Completed: _____

Searcher Prep & Review Time: _____

Online Time: _____

Type of Search

_____ NA Sequence (#)

_____ AA Sequence (#)

_____ Structure (#)

_____ Bibliographic

_____ Litigation

_____ Fulltext

_____ Other

Vendors and cost where applicable

STN _____ Dialog

_____ Questel/Orbit _____ Lexis/Nexis

_____ Westlaw _____ WWW/Internet

___In-house sequence systems

___Commercial ___Oligomer ___Score/Length

___Interference ___SPDI ___Encode/Transl

_____ Other (specify)

(FILE 'REGISTRY' ENTERED AT 14:55:26 ON 12 MAY 2005)

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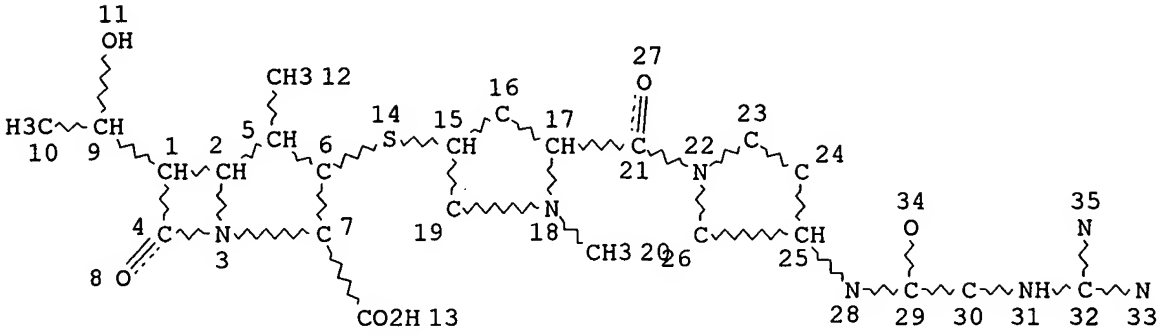


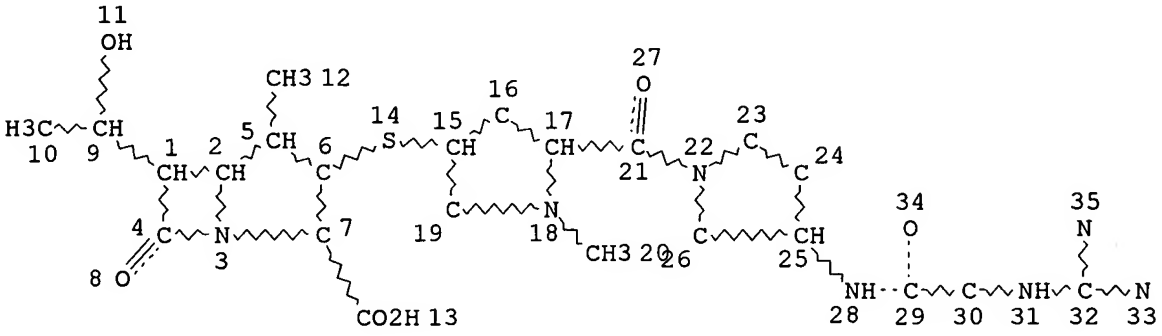
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 35

STEREO ATTRIBUTES: NONE

L2 (7) SEA FILE=REGISTRY SSS FUL L1

L3 STR



NODE ATTRIBUTES:
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CONNECT IS X2 RC AT 23
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 35

STEREO ATTRIBUTES: NONE

L4 7 SEA FILE=REGISTRY SUB=L2 SSS FUL L3

Searcher : Shears 571-272-2528

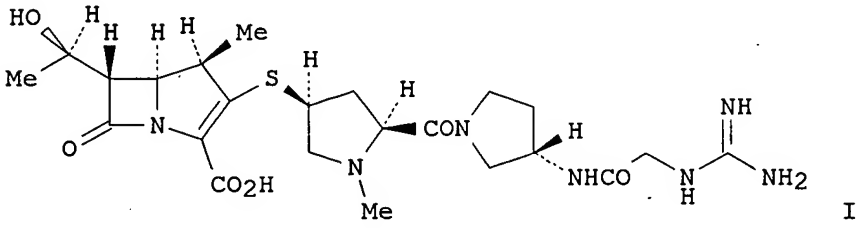
100.0% PROCESSED 7 ITERATIONS 7 ANSWERS
SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 15:02:45 ON 12 MAY 2005
L5 8 S L4/P

L5 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:182662 CAPLUS
DOCUMENT NUMBER: 142:279980
TITLE: Preparation of crystal of 1-methyl carbapenem compound
INVENTOR(S): Michida, Makoto; Nagao, Yuki
PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005019217	A1	20050303	WO 2004-JP12604	20040825
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2005097278	A2	20050414	JP 2004-243116	20040824
PRIORITY APPLN. INFO.:			JP 2003-299677 A	20030825

GI



I

AB There is provided a crystal of 1-methylcarbapenem compound (I), hydrate and/or ethanol solvate or a pharmacol. acceptable salt thereof, characterized in that it exhibits specific main peaks in a powder x-ray diffraction pattern obtained by the irradiation of a Cu-Kα line. Thus, 1 solution of 10.0 g (1R,5S,6S)-2-[(2S,4S)-2-[(3S)-3-[2-[2,3-bis(4-nitrobenzyloxycarbonyl)guanidino]acetylamino]pyrrolidin-1-ylcarbonyl]-1-methylpyrrolidin-4-ylthio]-6-[(1R)-1-hydroxyethyl]-1-

methyl-1-carbapen-2-em-3-carboxylic acid 4-nitrobenzyl ester in 120 mL THF containing 33% H2O was stirred in the presence of 3.13 g 7.5% Pd-C under H atmospheric at 20° for 24 h. The reaction mixture was filtered and the filtrate was washed with Et acetate. The aqueous layer was stirred with 4.3 g activated charcoal at room temperature for 30 min, filtered, concentrated, and treated with 100 mg NaHCO3 and 240 mL ethanol. The resulting suspension was left to stand at 0° for 16 h, stirred for 1 h, followed by filtering away precipitated crystals, washing with a 3:1 mixture of ethanol and water, and vacuum drying to give 4.35 g I ethanol solvate. I is useful for prevention and/or treatment of bacterial infections. A viral containing 250 mg I ethanol solvate was described.

IT **716339-38-7P**
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of crystal of 1-methylcarbapenem compound as antibacterial agent and characterization by powder x-ray diffraction)

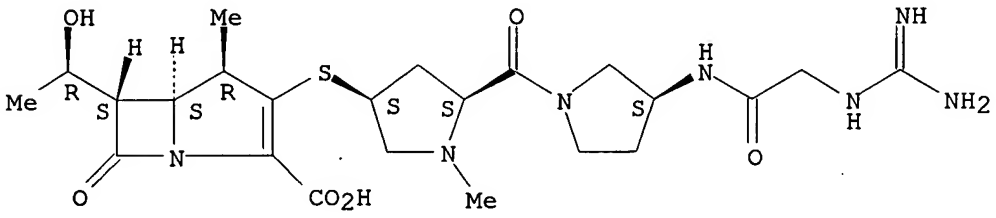
RN 716339-38-7 CAPLUS

CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)-, compd. with ethanol (1:1), trihydrate (9CI) (CA INDEX NAME)

CM 1

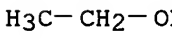
CRN 222400-20-6
CMF C23 H35 N7 O6 S

Absolute stereochemistry.



CM 2

CRN 64-17-5
CMF C2 H6 O



IT **847041-15-0P 847041-16-1P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of crystal of 1-methylcarbapenem compound as antibacterial agent and characterization by powder x-ray diffraction)

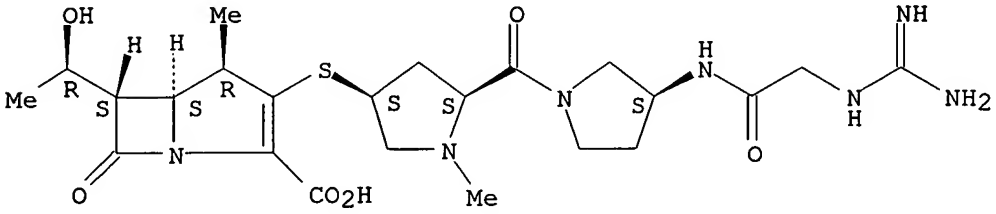
RN 847041-15-0 CAPLUS

CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)-, compd. with ethanol (1:1) (9CI) (CA INDEX NAME)

CM 1

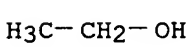
CRN 222400-20-6
CMF C23 H35 N7 O6 S

Absolute stereochemistry.



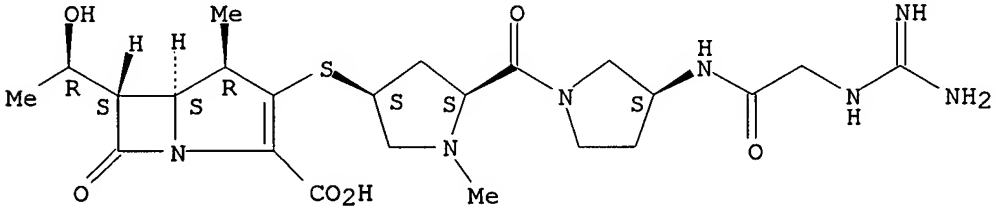
CM 2

CRN 64-17-5
CMF C2 H6 O



RN 847041-16-1 CAPLUS
CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, tetrahydrate, (4R,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 4 H_2O

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:550729 CAPLUS

DOCUMENT NUMBER: 141:94352
TITLE: Preparation of crystalline 1-methylcarbapenem derivatives
INVENTOR(S): Kawamoto, Isao; Shimoji, Yasuo; Fukuhara, Hiroshi
PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan
SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S. Ser. No. 407,546.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004132668	A1	20040708	US 2003-625317	20030723
WO 2001002401	A1	20010111	WO 2000-JP4496	20000706
W: AU, BR, CA, CN, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PL, RU, TR, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 2002128254	A1	20020912	US 2001-34548	20011228
US 2003232803	A1	20031218	US 2003-407546	20030403

PRIORITY APPLN. INFO.:

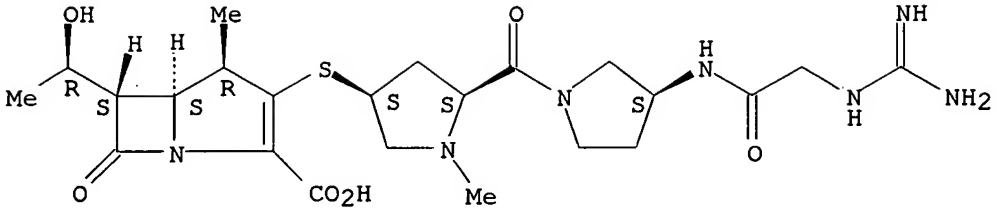
JP 1999-191368	A	19990706
WO 2000-JP4496	A1	20000706
US 2001-34548	B1	20011228
US 2003-407546	A2	20030403

AB This invention provides crystalline forms of a 1-methylcarbapenem derivative or its salts thereof. The crystalline forms of the 1-methylcarbapenem derivative exhibit excellent antibiotic activity against various bacterial strains and sufficient stability for practical use. (1R,5S,6S)-2-[(2S,4S)-2-[(3S)-3-(2-Guanidinoacetylamino)pyrrolidin-1-ylcarbonyl]-1-methylpyrrolidin-4-ylthio]-6-[(1R)-1-hydroxyethyl]-1-methyl-1-carbapen-2-em-3-carboxylic acid 0.5 EtOH solvate was prepared by the reduction of 4-nitrobenzyl (1R,5S,6S)-2-[(2S,4S)-2-[(3S)-3-[2-[2,3-bis(4-nitrobenzyloxycarbonyl)guanidino]-acetylamino]pyrrolidin-1-ylcarbonyl]-1-methyl-pyrrolidin-4-ylthio]-6-[(1R)-1-hydroxyethyl]-1-methyl-1-carbapen-2-em-3-carboxylate with 7.5% Pd/C. This compound had good stability at 40° and at 75% relative humidity.

IT **222400-20-6P 319449-32-6P 319449-33-7P 716339-38-7P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of crystalline methylcarbapenem derivs.)

RN 222400-20-6 CAPLUS
CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

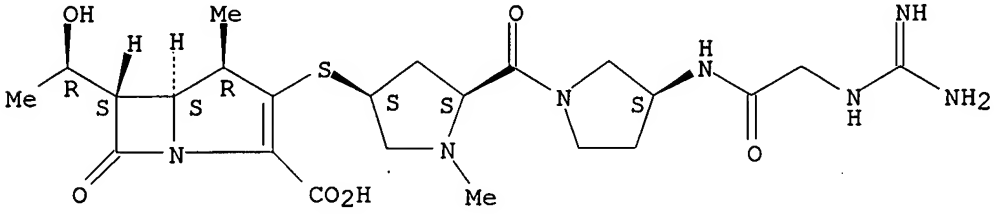


RN 319449-32-6 CAPLUS
CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)-, compd. with ethanol (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 222400-20-6
CMF C23 H35 N7 O6 S

Absolute stereochemistry.



CM 2

CRN 64-17-5
CMF C2 H6 O

RN 319449-33-7 CAPLUS
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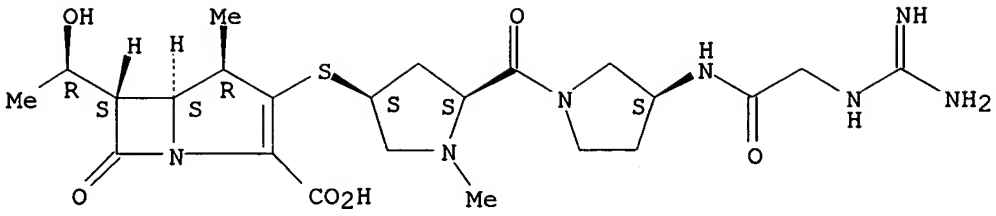
CM 1

CRN 222400-20-6
CMF C23 H35 N7 O6 S

Absolute stereochemistry.



CM 2

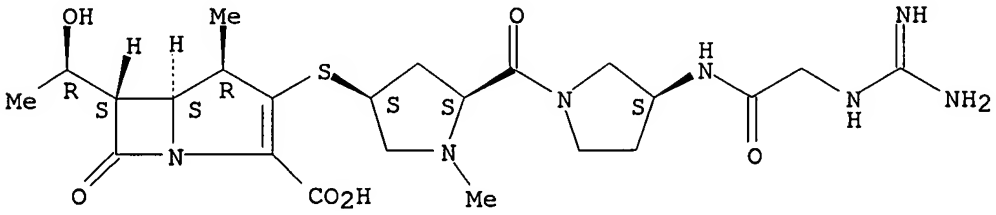
CRN 64-17-5
CMF C2 H6 O

RN 716339-38-7 CAPLUS
CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)-, compd. with ethanol (1:1), trihydrate (9CI) (CA INDEX NAME)

CM 1

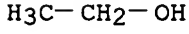
CRN 222400-20-6
CMF C23 H35 N7 O6 S

Absolute stereochemistry.



CM 2

CRN 64-17-5
CMF C2 H6 O



L5 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:512522 CAPLUS
DOCUMENT NUMBER: 140:25356
TITLE: Synthesis and structure-activity relationships of novel parenteral carbapenems, CS-023 (R-115685)

Searcher : Shears 571-272-2528

and related compounds containing an amidine moiety

AUTHOR(S): Kawamoto, Isao; Shimoji, Yasuo; Kanno, Osamu; Kojima, Katsuhiko; Ishikawa, Katsuya; Matsuyama, Emi; Ashida, Yuka; Shibayama, Takahiro; Fukuoka, Takashi; Ohya, Satoshi

CORPORATE SOURCE: Research Laboratories, Sankyo Co., Ltd., Tokyo, 140-8710, Japan

SOURCE: Journal of Antibiotics (2003), 56(6), 565-579
CODEN: JANTAJ; ISSN: 0021-8820

PUBLISHER: Japan Antibiotics Research Association

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 140:25356

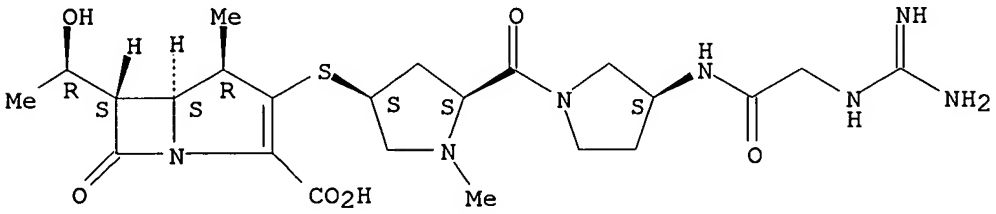
AB In order to design a new parenteral 1β-methylcarbapenem antibiotic which has a broad antibacterial spectrum and improved plasma half-life, a series of 1β-methylcarbapenems with 5-substituted pyrrolidine-3-ylthio groups including an amidine moiety at the C-2 position were synthesized and structure-activity relationships were investigated. Among those carbapenem derivs., CS-023 (R-115685) showed a broad spectrum and excellent antibacterial activity against Gram-pos. and Gram-neg. bacteria. This compound also showed sufficient dehydropeptidase-I (DHP-I) stability and high urinary recovery in animals after s.c. administration without cilastatin, a DHP-I inhibitor. Based on these characteristics, CS-023 was selected for further study.

IT **222400-20-6P**
RL: BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and structure-activity relationships of novel parenteral carbapenems and related compds. containing amidine moiety)

RN 222400-20-6 CAPLUS

CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:422924 CAPLUS

DOCUMENT NUMBER: 137:10956

TITLE: Storage-stable antibacterial agents containing crystals of carbapenem derivative

INVENTOR(S): Kawamoto, Isao; Shimoji, Yasuo; Fukuhara, Hiroshi

PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 19 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002161034	A2	20020604	JP 2001-274389	20010911
PRIORITY APPLN. INFO.:			JP 2000-278977 A	20000914

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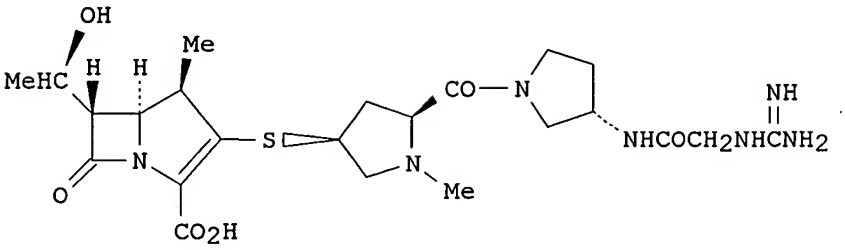


I

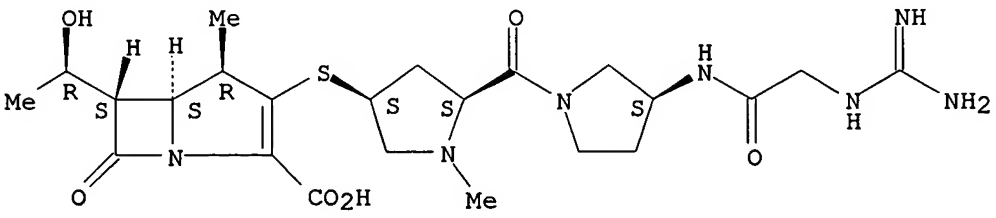
AB Antibacterial agents contain crystals of carbapenem derivative I or its pharmacol. acceptable salts. Thus, 4-nitrobenzyl (1R,5S,6S)-2-[(2S,4S)-2-[(3S)-3-[2-[2,3-bis(4-nitrobenzyloxycarbonyl)guanidino]acetylamino]pyrrolidin-1-ylcarbonyl]-1-methylpyrrolidin-4-ylthio]-6-[(1R)-1-hydroxyethyl]-1-methyl-1-carbapen-2-em-3-carboxylate was hydrogenated over Pd/C and treated with EtOH and dry ice to give I.0.5H2CO2.0.5EtOH crystals. The crystals were left at 40° and 75% relative humidity for 56 days to show residual I 92.9%, vs. 0.3, for freeze-dried I.

IT **222400-20-6P 319449-31-5P 319449-32-6P 319449-33-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of crystals of carbapenem derivative for storage-stable antibacterial agents)

RN 222400-20-6 CAPLUS

CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



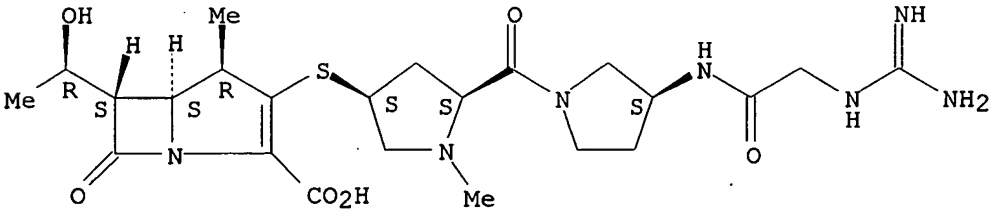
Searcher : Shears 571-272-2528

RN 319449-31-5 CAPLUS
CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)-, carbonate (salt), compd. with ethanol (2:1:1) (9CI) (CA INDEX NAME)

CM 1

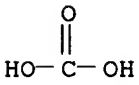
CRN 222400-20-6
CMF C23 H35 N7 O6 S

Absolute stereochemistry.



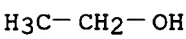
CM 2

CRN 463-79-6
CMF C H2 O3



CM 3

CRN 64-17-5
CMF C2 H6 O

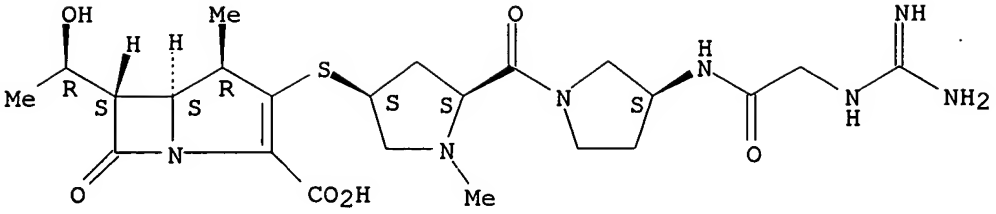


RN 319449-32-6 CAPLUS
CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)-, compd. with ethanol (2:1) (9CI) (CA INDEX NAME)

CM 1

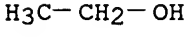
CRN 222400-20-6
CMF C23 H35 N7 O6 S

Absolute stereochemistry.



CM 2

CRN 64-17-5
CMF C2 H6 O

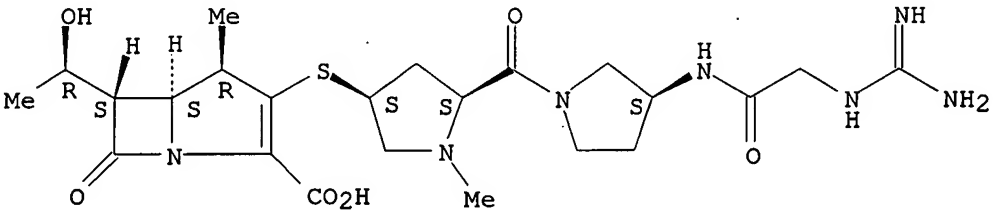


RN 319449-33-7 CAPLUS
CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)-, compd. with ethanol, hydrate (4:1:6) (9CI) (CA INDEX NAME)

CM 1

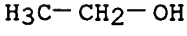
CRN 222400-20-6
CMF C23 H35 N7 O6 S

Absolute stereochemistry.



CM 2

CRN 64-17-5
CMF C2 H6 O



L5 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:935443 CAPLUS
DOCUMENT NUMBER: 136:58849
TITLE: Compositions and methods to improve the oral absorption of antimicrobial agents
INVENTOR(S): Choi, Seung-Ho; Lee, Jeoung-Soo; Keith, Dennis

PATENT ASSIGNEE(S): Cubist Pharmaceuticals, Inc., USA; International Health Management Associates, Inc.; University of Utah Research Foundation
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001097851	A2	20011227	WO 2001-US19625	20010618
WO 2001097851	A3	20020516		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6248360	B1	20010619	US 2000-598089	20000621
CA 2413251	AA	20011227	CA 2001-2413251	20010618
EP 1294361	A2	20030326	EP 2001-944619	20010618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012393	A	20030708	BR 2001-12393	20010618
JP 2003535911	T2	20031202	JP 2002-503335	20010618
NZ 523276	A	20050225	NZ 2001-523276	20010618
US 2003039956	A1	20030227	US 2001-888114	20010622
PRIORITY APPLN. INFO.:			US 2000-598089 A	20000621
			US 2001-829405 A	20010409
			US 2001-283976P P	20010416
			WO 2001-US19625 W	20010618

AB The present invention provides compns. and methods for increasing absorption of antibacterial agents, particularly third generation cephalosporin antibacterial agents, in oral dosage solid and/or suspension forms. Specifically, the composition is comprised of a biopolymer that is preferably swellable and/or mucoadhesive, an antimicrobial agent, and a cationic binding agent contained within the biopolymer such that the binding agent is ionically bound or complexed to at least one member selected from the group consisting of the biopolymer and the antimicrobial agent. A solution of 44.5 mg calcium chloride in 10 mL water and 1.0 g of ceftriaxone in 10 mL water was added gradually to a solution of 400 mg carrageenan and the dispersion was centrifuged and the supernatant was lyophilized. The resulting composition comprised carrageenan 27.7, ceftriaxone 1, and calcium chloride 3.1%. Plasma concentration of different antimicrobial-biopolymer complexes after oral administration to rats was measured.

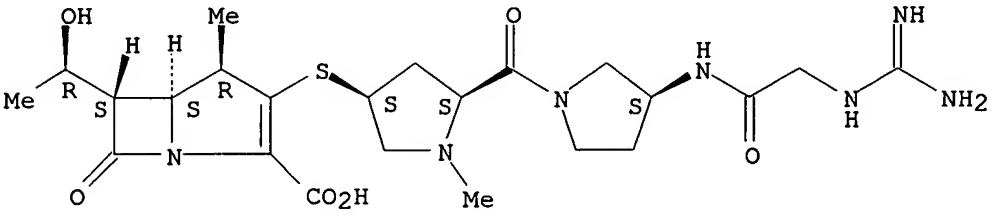
IT **222400-20-6DP**, R 115685, conjugates with biopolymers and cationic binding agents
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(compns. and methods to improve oral absorption of antimicrobial agents)

RN 222400-20-6 CAPLUS

CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:289966 CAPLUS

DOCUMENT NUMBER: 134:311032

TITLE: Preparation of acyl-protected mercaptopyrrolidines as intermediates for carbapenem antibiotics

INVENTOR(S): Kawamoto, Isao; Shimochi, Yasuo; Kanno, Osamu; Kojima, Katsuhiko

PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 32 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

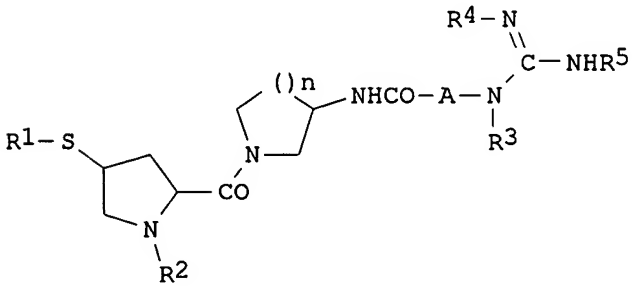
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
JP 2001114759	A2	20010424	JP 2000-242254		20000810
PRIORITY APPLN. INFO.:			JP 1999-228551	A	19990812

OTHER SOURCE(S): MARPAT 134:311032

GI



I

AB Mercaptopyrrolidines I [n = 0-2; A = (OH-substituted) C1-8 alkylene; R1 = acyl; R2 = C1-4 alkyl; R3 = H, C1-4 alkyl; R4, R5 = H, protecting group] are prepared Thus, (2S,4S)-4-acetylthio-1-methyl-2-pyrrolidinecarboxylic acid was treated with pivaloyl chloride and condensed with (S)-3-[2-[2,3-bis(4-nitrobenzyloxycarbonyl)guanidino]acetylamino]pyrrolidine 2HCl salt to give the corresponding amide, which was treated with hydrazine acetate in DMF at room temperature for 4 h and treated with carbapenemcarboxylic acid derivative

IT **319449-32-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of acyl-protected mercaptopyrrolidines as intermediates for carbapenem antibiotics)

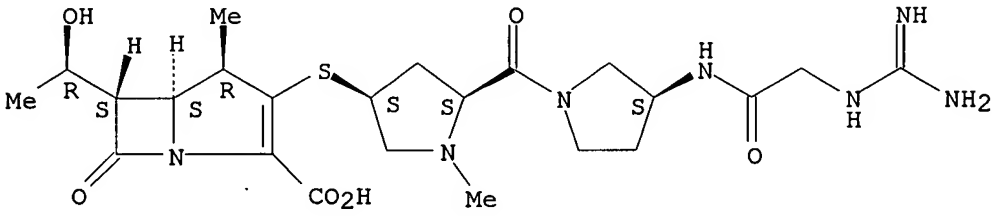
RN 319449-32-6 CAPLUS

CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)-, compd. with ethanol (2:1) (9CI) (CA INDEX NAME)

CM 1

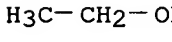
CRN 222400-20-6
CMF C23 H35 N7 O6 S

Absolute stereochemistry.



CM 2

CRN 64-17-5
CMF C2 H6 O



L5 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:31503 CAPLUS
DOCUMENT NUMBER: 134:100856
TITLE: Preparation and biological activity of crystalline 1-methylcarbapenem compounds as antibacterial agents
INVENTOR(S): Kawamoto, Isao; Shimoji, Yasuo; Fukuhara, Hiroshi
PATENT ASSIGNEE(S): Sankyo Company, Ltd., Japan
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001002401	A1	20010111	WO 2000-JP4496	20000706
W: AU, BR, CA, CN, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PL, RU, TR, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2378483	AA	20010111	CA 2000-2378483	20000706
JP 2001072681	A2	20010321	JP 2000-204430	20000706
JP 3476420	B2	20031210		
BR 2000012253	A	20020326	BR 2000-12253	20000706
EP 1193269	A1	20020403	EP 2000-944289	20000706
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
TR 200200100	T2	20020521	TR 2002-200200100	20000706
AU 758190	B2	20030320	AU 2000-58487	20000706
RU 2214411	C2	20031020	RU 2002-100058	20000706
NZ 516310	A	20040528	NZ 2000-516310	20000706
ZA 2001010413	A	20030319	ZA 2001-10413	20011219
US 2002128254	A1	20020912	US 2001-34548	20011228
NO 2002000030	A	20020305	NO 2002-30	20020104
US 2003158174	A1	20030821	US 2003-351944	20030127
US 2003232803	A1	20031218	US 2003-407546	20030403
US 2004132668	A1	20040708	US 2003-625317	20030723

PRIORITY APPLN. INFO.:	JP 1999-191368	A	19990706
	WO 2000-JP4496	W	20000706
	US 2001-34548	B3	20011228
	US 2003-407546	A2	20030403

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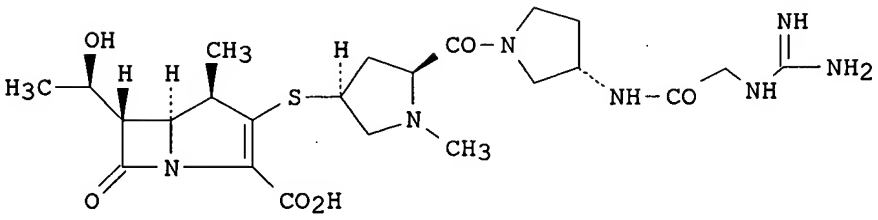


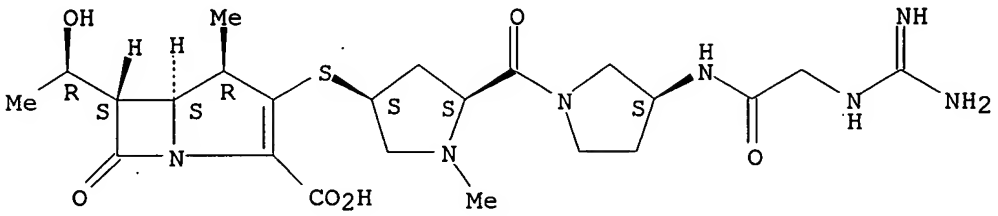
I

AB Crystals of compound I or pharmacol. acceptable salts thereof, which exhibit an excellent antimicrobial activity and are excellent in storage stability and handle ability as to be put into practical use as antimicrobial agents, are prepared

IT **222400-20-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and biol. activity of 1-methylcarbapenem as antibacterial

agents)
RN 222400-20-6 CAPLUS
CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

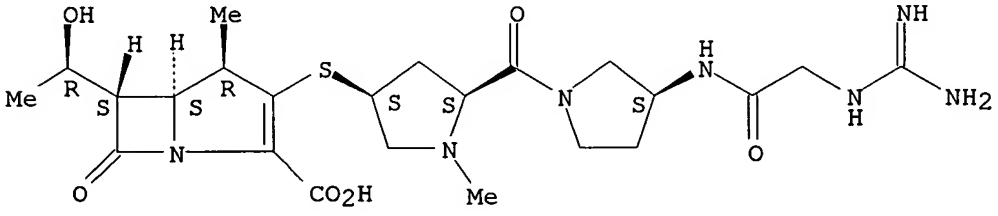


IT **319449-31-5P 319449-32-6P 319449-33-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and biol. activity of crystalline 1-methylcarbapenem compds. as
antibacterial agents)
RN 319449-31-5 CAPLUS
CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)-, carbonate (salt), compd. with ethanol (2:1:1) (9CI) (CA INDEX NAME)

CM 1

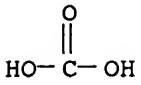
CRN 222400-20-6
CMF C23 H35 N7 O6 S

Absolute stereochemistry.



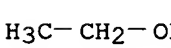
CM 2

CRN 463-79-6
CMF C H2 O3



CM 3

CRN 64-17-5
CMF C2 H6 O

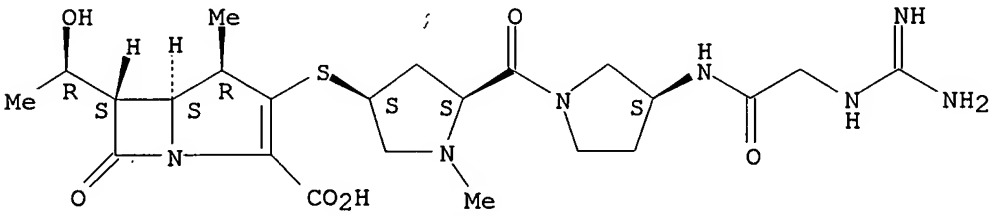


RN 319449-32-6 CAPLUS
CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)-, compd. with ethanol (2:1) (9CI) (CA INDEX NAME)

CM 1

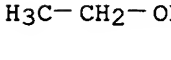
CRN 222400-20-6
CMF C23 H35 N7 O6 S

Absolute stereochemistry.



CM 2

CRN 64-17-5
CMF C2 H6 O

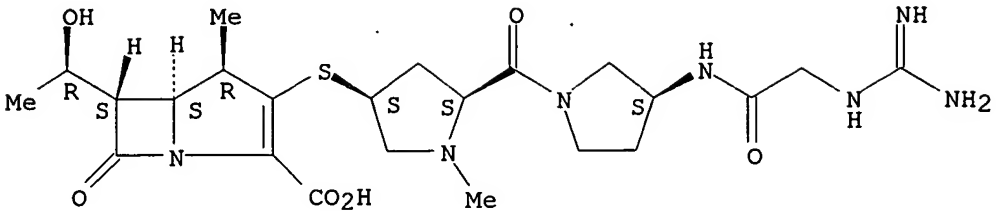


RN 319449-33-7 CAPLUS
CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)-, compd. with ethanol, hydrate (4:1:6) (9CI) (CA INDEX NAME)

CM 1

CRN 222400-20-6
CMF C23 H35 N7 O6 S

Absolute stereochemistry.



CM 2

CRN 64-17-5
CMF C2 H6 O

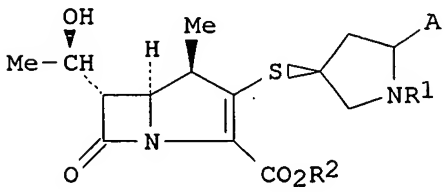
H_3C-CH_2-OH

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:188993 CAPLUS
DOCUMENT NUMBER: 130:262106
TITLE: Antibacterial 1-methylcarbapenem derivatives
INVENTOR(S): Kawamoto, Isao; Shimoji, Yasuo; Ishikawa, Katsunari; Kojima, Katsuhiko; Yasuda, Hiroshi; Oya, Tetsu; Utsui, Yukio
PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 121 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11071277	A2	19990316	JP 1998-171430	19980618
JP 2955276	B2	19991004		
PRIORITY APPLN. INFO.:			JP 1997-162311 A	19970619

GI



I

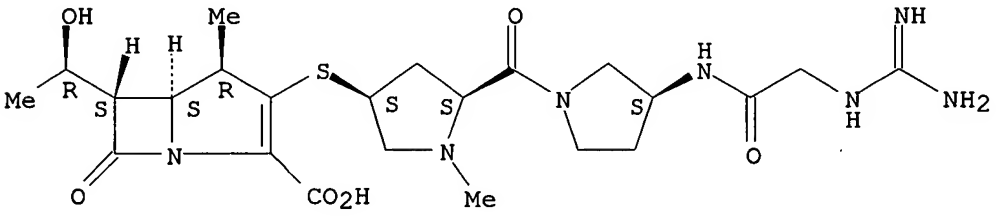
AB 1-Methylcarbapenem derivs. (I; R1 = H, low alkyl; R2 = H, ester residue; A = substituted prolylaminopyrrolidine-1-ylcarbonyl, substituted aminoalkanoylaminopyyrolidin-1-ylcarbonyl, 1-hydroxy-2-(substituted aminoalkylpyrrolidin-1-ylcarbonyl)ethyl, etc.) and their pharmacol. acceptable salts are claimed as antibacterials. Formulation examples of I injections, capsules, and tablets were given.

IT **222400-20-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antibacterial 1-methylcarbapenem derivs.)

RN 222400-20-6 CAPLUS

CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[(3S)-3-[[[(aminoiminomethyl)amino]acetyl]amino]-1-pyrrolidinyl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4R,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



FILE 'CAOLD' ENTERED AT 15:03:18 ON 12 MAY 2005
L6 0 S L4

FILE 'USPATFULL' ENTERED AT 15:03:25 ON 12 MAY 2005
L7 4 S L4/P

L7 ANSWER 1 OF 4 USPATFULL on STN
ACCESSION NUMBER: 2004:172504 USPATFULL
TITLE: Crystalline 1-methylcarbapenem derivatives
INVENTOR(S): Kawamoto, Isao, Tokyo, JAPAN
Shimoji, Yasuo, Tokyo, JAPAN
Fukuhara, Hiroshi, Yokohama-shi, JAPAN
PATENT ASSIGNEE(S): SANKYO COMPANY, LIMITED, Tokyo, JAPAN (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004132668	A1	20040708
APPLICATION INFO.:	US 2003-625317	A1	20030723 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-407546, filed on 3 Apr 2003, PENDING Continuation of Ser. No. US 2001-34548, filed on 28 Dec 2001, ABANDONED Continuation of Ser. No. WO 2000-JP4496, filed on 6 Jul 2000, UNKNOWN

NUMBER	DATE

PRIORITY INFORMATION: JP 1999-191368 19990706
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FRISHAUF, HOLTZ, GOODMAN & CHICK, PC, 767 THIRD AVENUE, 25TH FLOOR, NEW YORK, NY, 10017-2023
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 882
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides crystalline forms of a 1-methylcarbapenem derivative of formula (I) or of pharmaceutically acceptable salts thereof. ##STR1##

The crystalline forms of the 1-methylcarbapenem derivative exhibit excellent antibiotic activity against various bacterial strains and sufficient stability for practical use.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 2 OF 4 USPATFULL on STN
ACCESSION NUMBER: 2003:330588 USPATFULL
TITLE: Crystalline 1-methylcarbapenem derivatives
INVENTOR(S): Kawamoto, Isao, Tokyo, JAPAN
Shimoji, Yasuo, Tokyo, JAPAN
Fukuhara, Hiroshi, Yokohama-shi, JAPAN
PATENT ASSIGNEE(S): SANKYO COMPANY, LIMITED, Tokyo, JAPAN (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003232803	A1	20031218
APPLICATION INFO.:	US 2003-407546	A1	20030403 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-34548, filed on 28 Dec 2001, ABANDONED Continuation of Ser. No. WO 2000-JP4496, filed on 6 Jul 2000, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1999-191368	19990706

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FRISHAUF, HOLTZ, GOODMAN & CHICK, PC, 767 THIRD AVENUE, 25TH FLOOR, NEW YORK, NY, 10017-2023
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 891
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides crystalline forms of a 1-methylcarbapenem derivative of formula (I) or of pharmaceutically acceptable salts thereof. ##STR1##

The crystalline forms of the 1-methylcarbapenem derivative exhibit excellent antibiotic activity against various bacterial strains and sufficient stability for practical use.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 3 OF 4 USPATFULL on STN
ACCESSION NUMBER: 2003:226361 USPATFULL
TITLE: Crystalline 1-methylcarbapenem derivatives
INVENTOR(S): Kawamoto, Isao, Tokyo, JAPAN
Shimoji, Yasuo, Tokyo, JAPAN
Fukuhara, Hiroshi, Yokohama-shi, JAPAN
PATENT ASSIGNEE(S): SANKYO COMPANY, LIMITED, Tokyo, JAPAN, 103-8426 (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003158174	A1	20030821
APPLICATION INFO.:	US 2003-351944	A1	20030127 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-34548, filed on 28 Dec 2001, ABANDONED Continuation of Ser. No. WO 2000-JP4496, filed on 6 Jul 2000, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1999-191368	19990706

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FRISHAUF, HOLTZ, GOODMAN & CHICK, PC, 767 THIRD AVENUE, 25TH FLOOR, NEW YORK, NY, 10017-2023
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 884
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides crystalline forms of a 1-methylcarbapenem derivative of formula (I) or of pharmaceutically acceptable salts thereof. ##STR1##

The crystalline forms of the 1 -methylcarbapenem derivative exhibit excellent antibiotic activity against various bacterial strains and sufficient stability for practical use.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 4 OF 4 USPATFULL on STN
ACCESSION NUMBER: 2002:236056 USPATFULL
TITLE: Crystalline 1-methylcarbapenem derivatives
INVENTOR(S): Kawamoto, Isao, Tokyo, JAPAN
Shimoji, Yasuo, Tokyo, JAPAN
Fukuhara, Hiroshi, Yokohama-shi, JAPAN
PATENT ASSIGNEE(S): SANKYO COMPANY, LIMITED, Tokyo, JAPAN (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002128254	A1	20020912
APPLICATION INFO.:	US 2001-34548	A1	20011228 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. WO 2000-JP4496, filed on 6 Jul 2000, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1999-191368	19990706

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FRISHAUF, HOLTZ, GOODMAN &, LANGER & CHICK, PC, 767 THIRD AVENUE, 25TH FLOOR, NEW YORK, NY, 10017-2023
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 885
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides crystalline forms of a 1-methylcarbapenem derivative of formula (I) or of pharmaceutically acceptable salts thereof. ##STR1##

The crystalline forms of the 1-methylcarbapenem derivative exhibit excellent antibiotic activity against various bacterial strains and sufficient stability for practical use.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

(FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 15:03:47 ON 12 MAY 2005)
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L9 4 DUP REM L8 (0 DUPLICATES REMOVED)

L9 ANSWER 1 OF 4 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:421410 BIOSIS
DOCUMENT NUMBER: PREV200400424701
TITLE: CS-023 (R-115685), a novel carbapenem with enhanced in vitro activity against oxacillin-resistant staphylococci and Pseudomonas aeruginosa.
AUTHOR(S): Thomson, Kenneth S. [Reprint Author]; Moland, Ellen Smith
CORPORATE SOURCE: Sch MedDept Med Microbiol and ImmunolCtr Res Antiinfect and Biotechnol, Creighton Univ, Omaha, NE, 68178, USA kstaac@creighton.edu
SOURCE: Journal of Antimicrobial Chemotherapy, (August 2004) Vol. 54, No. 2, pp. 557-562. print. ISSN: 0305-7453 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Nov 2004
Last Updated on STN: 3 Nov 2004
AB Objective: To compare the in vitro activities of the carbapenem, CS-023, four representative beta-lactam antibiotics and levofloxacin, against 970 Gram-positive or Gram-negative US clinical isolates. Methods: Susceptibilities of bacteria chosen for their varying levels of resistance to the comparator agents were determined by NCCLS microdilution methodology. Results: CS-023 exhibited activity comparable to that of imipenem against most Gram-positive isolates, but was apprx8-fold more potent against oxacillin-resistant staphylococci. It was comparable to meropenem against most Gram-negative isolates, but was 4- to 8-fold more potent against five isolates of meropenem-resistant Pseudomonas aeruginosa. Conclusions: If tissue and body fluid concentrations >8 mg/L can safely be achieved, further studies of CS-023 are warranted to determine its clinical efficacy.

L9 ANSWER 2 OF 4 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:480343 BIOSIS

DOCUMENT NUMBER: PREV200300480343
TITLE: Synthesis and structure-activity relationships of novel parenteral carbapenems, CS-023 (R-115685) and related compounds containing an amidine moiety.
AUTHOR(S): Kawamoto, Isao; Shimoji, Yasuo; Kanno, Osamu [Reprint Author]; Kojima, Katsuhiko; Ishikawa, Katsuya; Matsuyama, Emi; Ashida, Yuka; Shibayama, Takahiro; Fukuoka, Takashi; Ohya, Satoshi
CORPORATE SOURCE: Research Laboratories, Sankyo Co., Ltd., 1-2-58 Hiromachi, Shinagawa-ku, Tokyo, 140-8710, Japan kannoo@shina.sankyo.co.jp
SOURCE: Journal of Antibiotics (Tokyo), (June 2003) Vol. 56, No. 6, pp. 565-579. print.
CODEN: JANTAJ. ISSN: 0021-8820.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Oct 2003
Last Updated on STN: 15 Oct 2003

AB In order to design a new parenteral 1beta-methylcarbapenem antibiotic which has a broad antibacterial spectrum and improved plasma half-life, a series of 1beta-methylcarbapenems with 5-substituted pyrrolidine-3-ylthio groups including an amidine moiety at the C-2 position have been synthesized and structure-activity relationships were investigated. Among those carbapenem derivatives, CS-023 (R-115685) showed a broad spectrum and excellent antibacterial activity against Gram-positive and Gram-negative bacteria. This compound also showed sufficient dehydropeptidase-I (DHP-I) stability and high urinary recovery in animals after subcutaneous administration without cilastatin, a DHP-I inhibitor. Based on these characteristics, CS-023 was selected for further study.

L9 ANSWER 3 OF 4 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:555359 BIOSIS
DOCUMENT NUMBER: PREV200200555359
TITLE: CS-023 (R-115685), a novel parenteral carbapenem: I. In vitro and in vivo pharmacodynamic (PD) evaluations against Pseudomonas aeruginosa.
AUTHOR(S): Koga, T. [Reprint author]; Fukuoka, T. [Reprint author]; Ishii, C. [Reprint author]; Kitayama, A. [Reprint author]; Abe, T. [Reprint author]; Harasaki, T. [Reprint author]; Nakagawa, M. [Reprint author]; Matsushita, Y. [Reprint author]; Shibayama, T. [Reprint author]; Hirota, T. [Reprint author]; Ohya, S. [Reprint author]; Kuwahara, S.
CORPORATE SOURCE: Res. Labs., Sankyo Co., Ltd., Tokyo, Japan
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2001) Vol. 41, pp. 209. print.
Meeting Info.: 41st Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy. Chicago, Illinois, USA. September 22-25, 2001.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Oct 2002
Last Updated on STN: 30 Dec 2002

AB Background: CS-023 (CS) has potent antibacterial activity against P. aeruginosa. The predicted human plasma half-life of CS (2.3 h) is

longer than those of imipenem (IPM, 1.0 h) and meropenem (MEPM, 0.9 h). These characteristics of CS could provide more effective therapy and better patients' compliance compared with IPM and MEPM. The activity of CS against P. aeruginosa was evaluated using in vitro and in vivo PD models. Methods: Bactericidal activities of the drugs were evaluated using in vitro PD models simulating the clinical doses shown in the table. The following three parameters were used for the evaluation: (i) maximal decrease (Max kill), (ii) final reduction (Fin CFU rd), and (iii) area between the killing curve and detection limit (AUC). The efficacy of CS for the thigh muscle infection was also evaluated using the in vivo PD model at a simulated single dose of 125-500 mg in neutropenic and normal mice. Results: The results in the in vitro PD models are shown in the table. In the in vivo PD models, CS suppressed the bacterial growth in the thighs at simulated doses of gtoreq350 mg in neutropenic mice, and reduced the viable cells significantly compared with those at initiation of therapy at simulated doses of gtoreq125 mg in normal mice. Conclusion: These results strongly suggest that CS could be a promising candidate with fewer dosings or lower dosage compared with IPM and MEPM.

L9 ANSWER 4 OF 4 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:555360 BIOSIS
DOCUMENT NUMBER: PREV200200555360
TITLE: CS-023 (R-115685), a novel parenteral carbapenem: II. In vitro and in vivo activities against methicillin-resistant Staphylococcus aureus.
AUTHOR(S): Fukuoka, T. [Reprint author]; Koga, T. [Reprint author]; Ishii, C. [Reprint author]; Kitayama, A. [Reprint author]; Namba, E. [Reprint author]; Abe, T. [Reprint author]; Nakagawa, M. [Reprint author]; Matsushita, Y. [Reprint author]; Shibayama, T. [Reprint author]; Hirota, T. [Reprint author]; Ohya, S. [Reprint author]; Kuwahara, S.
CORPORATE SOURCE: Res. Labs., Sankyo Co., Ltd., Tokyo, Japan
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2001) Vol. 41, pp. 209. print.
Meeting Info.: 41st Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy. Chicago, Illinois, USA. September 22-25, 2001.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Oct 2002
Last Updated on STN: 30 Dec 2002

AB Background: CS-023 (CS) has more potent activity against MRSA than imipenem (IPM) and meropenem (MEPM). We evaluated the mode of action, and in vitro and in vivo activities of CS against MRSA using pharmacodynamic (PD) models. Methods: The binding affinities of CS, IPM, and MEPM to penicillin-binding protein 2a (PBP2a) were measured by competition assay with 14C-benzylpenicillin;MICs (mug/ml) of CS, IPM, and MEPM for the strain used were 8, 32, and 32, respectively. In vitro PD were analyzed by simulating the clinical doses shown in the table. The three parameters were used for the evaluation: (i) maximal decrease, (ii) final reduction, and (iii) area between the killing curve and detection limit. The efficacy of CS for the sepsis model with a clinical isolate (MIC of CS=8) was also evaluated using the in vivo PD model simulating a single dose of 125-500 mg in

neutropenic and normal mice. Results: The IC50 (mug/ml) of CS (5.3) to PBP2a was extremely lower than those of IPM (170) and MEPM (130). The results in the in vitro PD models are shown in the table. In the in vivo PD models, CS showed more than 50% survivorship at simulated doses of gtoreq125 mg in neutropenic mice, and in normal mice. Conclusion: These results suggest that the CS could be active against MRSA due to its high affinity to PBP2a, and be a promising candidate with efficacy against MRSA infections.

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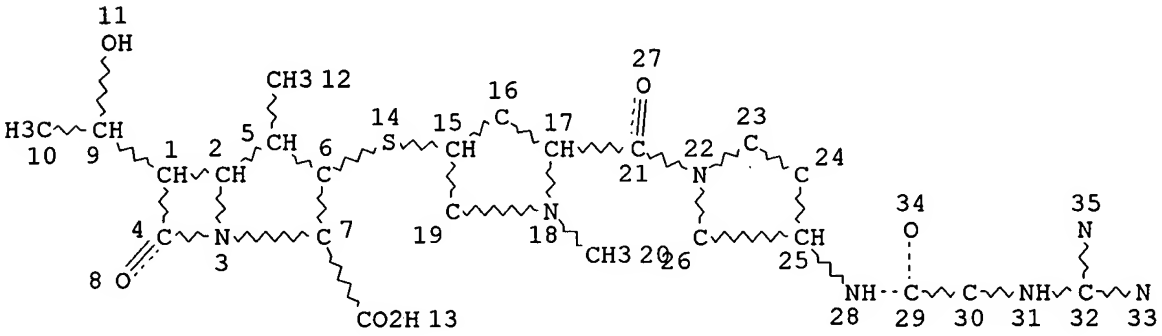

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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 35

STEREO ATTRIBUTES: NONE
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L11 ANSWER 1 OF 1 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:25356 CASREACT
TITLE: Synthesis and structure-activity relationships of novel parenteral carbapenems, CS-023 (R-115685) and related compounds containing an amidine moiety
AUTHOR(S): Kawamoto, Isao; Shimoji, Yasuo; Kanno, Osamu; Kojima, Katsuhiko; Ishikawa, Katsuya; Matsuyama, Emi; Ashida, Yuka; Shibayama, Takahiro; Fukuoka, Takashi; Ohya, Satoshi
CORPORATE SOURCE: Research Laboratories, Sankyo Co., Ltd., Tokyo, 140-8710, Japan
SOURCE: Journal of Antibiotics (2003), 56(6), 565-579
CODEN: JANTAJ; ISSN: 0021-8820

PUBLISHER: Japan Antibiotics Research Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In order to design a new parenteral 1β-methylcarbapenem antibiotic which has a broad antibacterial spectrum and improved plasma half-life, a series of 1β-methylcarbapenems with 5-substituted pyrrolidine-3-ylthio groups including an amidine moiety at the C-2 position were synthesized and structure-activity relationships were investigated. Among those carbapenem derivs., CS-023 (R-115685) showed a broad spectrum and excellent antibacterial activity against Gram-pos. and Gram-neg. bacteria. This compound also showed sufficient dehydropeptidase-I (DHP-I) stability and high urinary recovery in animals after s.c. administration without cilastatin, a DHP-I inhibitor. Based on these characteristics, CS-023 was selected for further study.

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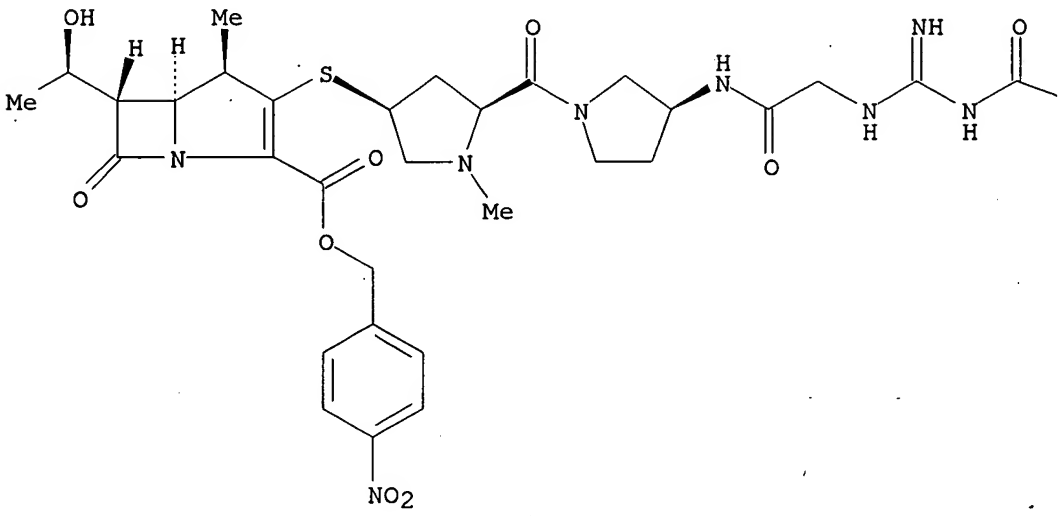

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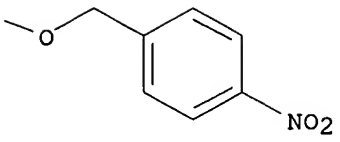

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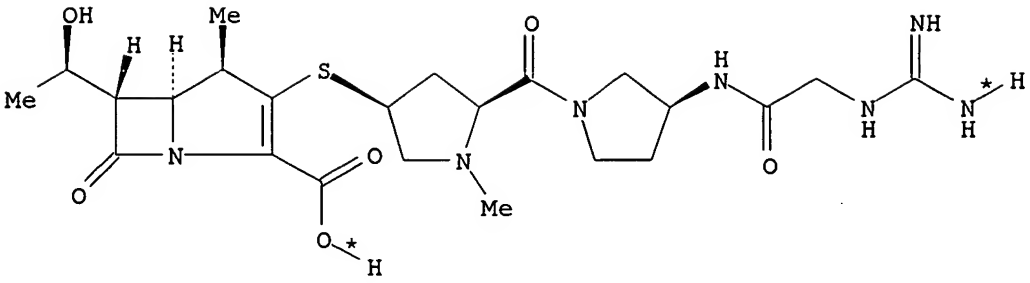

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STAGE(2)
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PRO U **222400-20-6**

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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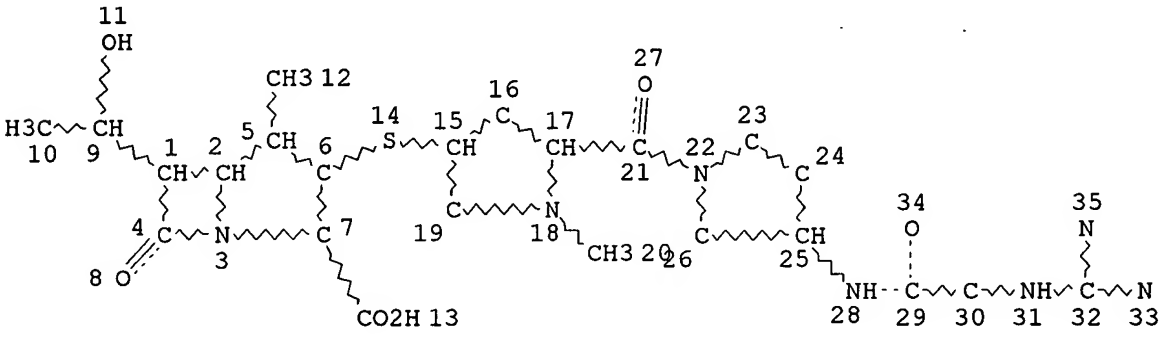

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NUMBER OF NODES IS 35

STEREO ATTRIBUTES: NONE
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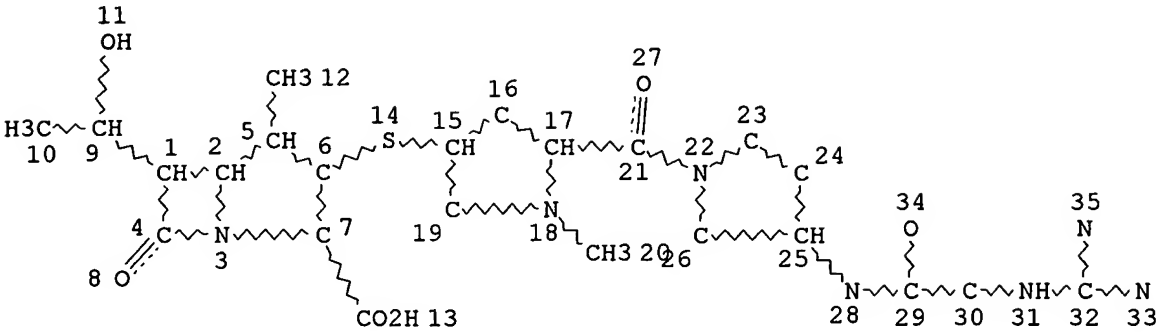

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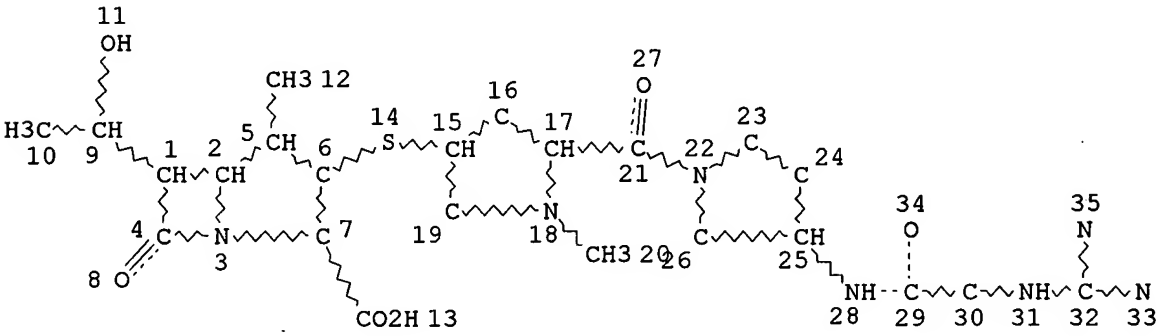

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  35

STEREO ATTRIBUTES: NONE
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L4              7 SEA SUB=L2 SSS FUL L3
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Searcher : Shears 571-272-2528